

REMARKS

Claims 28, 29, 31, 32 and 44-47 are pending. Claims 28, 29, 31, 32 and 44-47 are presented for further consideration.

The rejection of claims 28, 29, 31, 32 and 44-47 are rejected under Section 102(a) based on Harris *et al.* (WO 94/09136, published 4/28/1994) has been maintained. Applicant previously forwarded a Rule 131 declaration of Dr. Hans Hansen, one of the inventors, which showed that applicant had reduced the present invention to practice prior to the effective date of the cited Harris document. In addition, applicant presented the declaration of Mr. Bryan Wilson, documenting attempts to obtain a similar declaration from Dr. Leung, the other co-inventor.

The examiner found these declarations ineffective to overcome the applied reference because the Declaration had not executed by one of the named inventors, Dr. Shui-On- Leung. Applicant subsequently filed, on August 30, 2010, a petition under 37 CFR 1.183, requesting waiver of the requirement that the declaration be signed by all inventors. A decision was mailed on December 13, 2010, dismissing applicants' petition.

The decision on applicant's petition stated the following:

Since petitioner is alleging that Leung is refusing to sign the declaration, at the very least, petitioner should mail correspondence to the non signing inventor's last known address, return receipt and/or forwarding address requested. If a forwarding address is provided, petitioner should then mail a complete copy of the declaration to Leung's address, return receipt requested, along with a cover letter of instructions which includes a deadline or a statement that no response will constitute a refusal. This sort of ultimatum lends support to a finding of refusal by conduct.

On March 15, 2011, the undersigned sent, via Federal Express International Priority Service, a final revised version of the declaration which included all of Dr. Leung's input as conveyed to the undersigned by Dr. Leung's attorney, Gregory Lantier. Applicant used the most recent address known to them for Dr. Leung, which was given by Dr. Leung in an affirmation filed on October 30, 2007, in Action No. 1767 of 2007, in the High Court of the

Hong Kong Special Administrative Region. This affirmation was filed in connection with ongoing litigation with Immunomedics.

The declaration which was sent to Dr. Leung was accompanied by a cover letter which stated that "If you do not return the declaration within one month, *i.e.*, by April 14, 2011, we shall take that as a refusal on your part to execute the declaration in accordance with the terms of your employment agreement with Immunomedics, Inc." Also included was a prepaid envelope for return of the executed declaration.

On March 18, 2011, the undersigned was informed by Federal Express that Dr. Leung had moved, and was asked whether an undated address could be provided. The undersigned contacted Gregory Lantier, however he was unable to share a more current address for Dr. Leung. Subsequently, the Federal Express package was returned to the undersigned, with a notation that Dr. Leung had moved, dated March 18, 2011. A copy of the declaration and the cover letter, as well as the Federal Express label, and a copy of the stamped returned package are attached in Appendix A.

Upon learning that Dr. Leung had moved, the undersigned sent, on March 23, 2011, a second package, using the USPS International Guaranteed service, using a newly dated cover letter, and again providing a prepaid envelope for return of the enclosed declaration. The reason for this second attempt was to have a package that would route through the Hong Kong postal service, which might know of a forwarding address for Dr. Leung. The undersigned contacted the help line of the USPS International branch, and also had a staff member hand carry the package to the Post Office to ask whether the package would be forwarded by the Hong Kong postal service, to ascertain what would happen vis-à-vis forwarding in Hong Kong. The reply in both instances was that the forwarding of mail by a foreign postal service was not within their control, and there was no way of ascertaining whether the package would be forwarded. This second package also was returned to the undersigned, with the notation "addressee unknown." A copy of the cover letter, as well as

the USPS Express Mail label, and a copy of the stamped returned package are attached in Appendix B.¹

Accordingly, the undersigned now has provided an ultimatum as directed by the Board which would support "a finding of refusal by conduct." The undersigned has tried diligently to present the declarations to Dr. Leung for signature. Justice demands that the USPTO now accept the proffered evidence that a declaration executed by Dr. Leung cannot be obtained, and accept the declaration of Dr. Hansen with respect to the rejection based on Harris. Indeed, this was the response of the Senior Petitions Examiner in SN 11/676,466, when presented with a request that the requirement that a declaration under 37 CFR 1.131 be signed by all of the inventors in an application be waived.² SN 11/676,466 and the present case share priority to the same parent case. In that case, Applicant used the declaration of Bryan Wilson, which was submitted in this case in support of its petition to proceed without Dr. Leung's signature on his Rule 131 declaration. In SN 11/676,466, applicant's petition was granted. The Senior Petitions Examiner who signed the decision on petition in that case found that:

Petitioner has established that the non-signing inventor, Shui-on Leung, has refused to sign the declaration. Therefore, in the interest of justice, the signature requirement of Dr. Leung on the declaration under 37 CFR 1.131 is waived.

It is submitted that applicant has done all within its power to obtain Dr. Leung's signature on his declaration, and have even taken the additional steps set forth by Petitions Examiner Carl Friedman in his decision on petition, which were not required by Senior Petitions Attorney Shirene Brantley.

As previously noted, the declaration of Dr. Hansen is sufficient to establish prior reduction to practice of the presently claimed subject matter, thereby removing Harris as a reference. The examiner has not set forth any substantive basis for maintaining the rejection based on Harris, merely the procedural one based on the absence of Dr. Leung's declaration. Accordingly, no further comment is necessary on the part of applicant.

¹ The declaration is not included in Appendix B, as it is the same as the one sent via Federal Express.

² Senior Petitions Attorney Shirene Willis Brantley decided the petition in SN 11/676,466, and Petitions Examiner Carl Friedman decided the petition in the present case.

Claims 44-47 are rejected under Section 102(b) based on Adair *et al.* (WO 91/09967). The examiner cites Adair (WO 91/09967) as teaching a method of designing humanized heavy and light chain variable domain amino acid sequences of murine monoclonal antibody B72.3 comprising comparing the light and heavy chain variable domain sequences of B72.3 with the light and heavy chain sequences of two or more human antibodies (*e.g.*, those in Kabat), wherein the human REI light chain frameworks are selected and the human EU heavy chain frameworks are selected for FR1, FR2 and FR3 and a human consensus heavy chain FR4 was selected and the selected human frameworks are incorporated with the corresponding light and heavy chain CDRs of B72.3 and the light chain mouse residue at position 48 (2 amino acids from CDR2) and the heavy chain mouse residues at position 73, which is close to both CDRs 1 and 3 and could have a detrimental effect on antigen binding were retained in the humanized B72.3 antibody (*i.e.*, residues predicted to have contacts with the CDRs and within a 4.5 Angstrom radius of any atoms within the CDRs).

Claims 44-47 all recite "selecting framework regions from a first human antibody for the light chain and from second and third human antibodies for the heavy chain based on the sequence comparison, wherein the heavy chain FR1, FR2 and FR3 are selected from the second human antibody and FR4 is selected from the third human antibody." The examiner admits in the statement of rejection that "the human REI light chain frameworks are selected and the human EU heavy chain frameworks are selected for FR1, FR2 and FR3 and a human consensus heavy chain FR4 was selected." Thus, even the examiner does not state that FR4 was selected from a third antibody, but rather that a "consensus" FR4 is selected. A consensus sequence refers to the most common nucleotide or amino acid at a particular position after multiple sequences are aligned, *i.e.*, it is a way of representing the results of a multiple sequence alignments, where related sequences are compared to each other. A consensus sequence cannot be "selected from a third antibody" as presently claimed.

Adair did not compare the amino acid sequences of the light and heavy chain variable domains of a monoclonal antibody to be humanized with the amino acid

sequences of the light and heavy chain variable domains of two or more human antibodies, then select framework regions from a first human antibody for the light chain, and from second and third human antibodies for the heavy chain based on the sequence comparison, wherein the heavy chain FR1, FR2 and FR3 are selected from the second human antibody and FR4 is selected from the third human antibody, and then incorporate the framework regions selected with the corresponding light and heavy chain complementarity determining regions of the monoclonal antibody to be humanized, to design a humanized light and heavy chain variable domain amino acid sequences. Adair used a consensus FR4, and therefore does not teach "FR4 is selected from the third human antibody" as presently claimed. On this basis alone, the rejection under Section 102 must fail.

If there are any problems with this response, or if the examiner believes that a telephone interview would advance the prosecution of the present application, Applicant's attorney would appreciate a telephone call. In view of the foregoing, it is believed none of the references, taken singly or in combination, disclose the claimed invention. Accordingly, this application is believed to be in condition for allowance, the notice of which is respectfully requested.

Respectfully submitted,

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DATE

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